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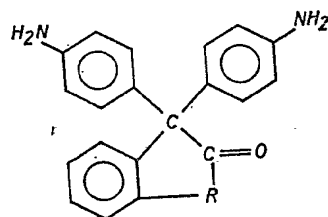


(54) OXINDOLE DIAMINE DERIVATIVES AND A PROCESS  
 FOR THEIR PREPARATION

(71) We, CIBA - GEIGY AG., a Swiss Body Corporate, of Basle, Switzerland, do hereby declare the invention, for which we pray that a patent may be granted to us, and the method by which it is to be performed, to be particularly described in and by the following statement:—

This invention relates to novel oxindole diamine derivatives and to a process for the preparation of these compounds.

According to the present invention, there is provided a derivative having the formula:—



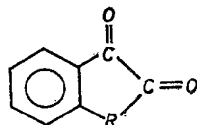
I

wherein R is an N - (lower)alkyl or an N-aryl residue.

The (lower)alkyl groups employed herein may be either straight or branched chain alkyl groups having up to six carbon atoms. Examples of such groups are methyl, ethyl, propyl, isopropyl, butyl, t-butyl, pentyl and hexyl groups. The aryl groups employed include phenyl; phenyl substituted with one or more alkyl groups such as methyl, ethyl, and propyl or with one or more halogen groups such as chlorine or bromine and nitro groups; and naphthyl, anthryl and phenanthryl groups.

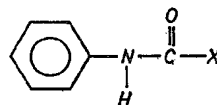
The compounds of formula I may be prepared by the following procedure which comprises the following steps:—

(a) reacting a derivative of the formula



II

wherein R is an N-(lower) alkyl or an N-aryl residue with an anilide of the formula



III

wherein X is an alkyl residue of from 1 to 6 carbon atoms, or an aryl or anilino residue in the presence of a Friedel Crafts catalyst in an inert solvent at a temperature of from 50°C. to 150°C., the derivative of formula II being present in an amount ranging from 1% to 15% by weight of the total reaction mixture, the anilide being present in at least a mole equivalent amount based on the amount of the derivative of formula II, and the Friedel Crafts catalyst being present in an amount ranging from 2 to 10 mole equivalents based on the amount of the derivative of formula II present in the reaction mixture;

(b) precipitating the resultant reaction product from step (a) by dilution with a solvent which is not a solvent for the reaction product from step (a);

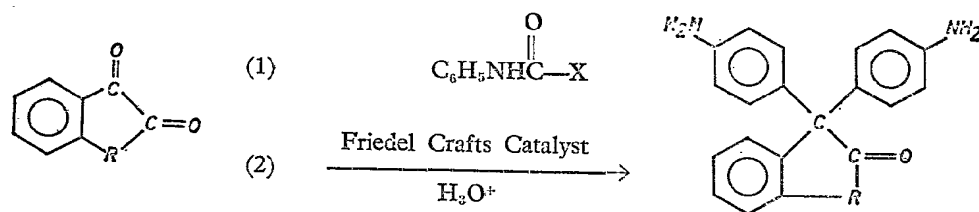
(c) hydrolyzing the reaction product in an aqueous acidic solution.

Preferably, the solvent in step (b) is water, an aliphatic alkane or a mixture thereof.

Isatin derivatives of formula II wherein R is an N-aryl or an N-alkyl residue may be prepared as indicated in Belstein, 21, page 447; 1st Supplement page 355; 2nd Supplement, page 337. The reference describes the preparation of 1-phenyl isatin by reacting oxalyl chloride with diphenylamine. By following the procedure of this reference but substituting other aryl or alkylsubstituted phenylamines for the diphenyl amine, the appropriate isatin derivative is obtained. Thus, examples of amines which may be substituted for diphenylamine include N-methylaniline, N-ethylaniline, N-propylaniline, N-butylaniline, N-isopropylaniline and N-hexylaniline, as well as N-anthrylaniline and N-naphthylaniline.

In this context, the disclosure in German Patent 515,542 is also pertinent.

The process of this invention may be represented by the following chemical reaction scheme:—



5 wherein R and X are as defined previously.

The reaction as indicated in step (1) may be carried out at a temperature of from 50°C to 150°C. and preferably from 90°C to 120°C.

10 Most Friedel Crafts type solvents which have boiling points within the temperature range above stated or higher and which are inert to the reactants employed are suitable for this reaction.

15 Examples of suitable solvents are tetrachloroethane, trichloroethane, dichloroethane, and nitrobenzene.

In the third step of the reaction, the reacted anilide may be hydrolyzed to yield the derivative of formula I. The hydrolysis may be carried out at reflux temperature in the aqueous acidic solution. Acids which may be used include sulphuric acid, hydrochloric acid and toluene sulphonic acid, alone or in combination with acetic acid. The preferred aqueous acidic solution consists of water, sulphuric acid and acetic acid.

20 The concentration of the derivative of formula II in the reaction mixture may range from 1 to 15% by weight of the total reaction mixture and is preferably in the range of from 2 to 7%.

It is generally preferable to have a slight excess of anilide in the reaction mixture. Thus, at least 1 to 5 mole equivalents of anilide is used per mole equivalent of the derivative of formula II and preferably from 1 to 2 mole equivalents. The amount of Friedel-Crafts catalyst present in the reaction consists of from 2 to 10 mole equivalents based on the amount of the derivative of formula II and preferably from 2 to 6 mole equivalents.

Examples of the Friedel-Crafts catalyst are those which are well known in the art and include aluminium chloride, aluminium bromide, ferric chloride, ferric bromide, zinc chloride, titanium tetrachloride, boron trifluoride, hydrogen fluoride, stannic chloride, sulphuric acid and polyphosphoric acid.

50 Examples of the anilide compounds of formula III wherein X is alkyl of from 1 to 6 carbonatoms are acetanilide, propionanilide, isopropionanilide, butyranilide, pentan-

anilide, and hexananilide; and examples of compounds of formula I wherein X is aryl are benzanilide and naphthanilide.

In a most preferred embodiment of the process of this invention, a solution of 0.05 equivalents of the derivative of formula II, 0.06 mole equivalents of the carbanilide, and 0.30 moles of aluminum chloride in 200 ml. of nitrobenzene are maintained at 100°C for about 12 hours. The cooled solution is poured into one litre of ice water and 600 ml. of hexane to precipitate the product. After filtering, the product is suspended in 200 ml. of acetic acid, 5 ml. of water, and 20 ml. of sulphuric acid. This solution is refluxed for approximately 24 hours, cooled and filtered. This refluxing hydrolyzes the reacted anilide and yields the desired oxindole diamine derivative. The filtrate containing the oxindole diamine derivative is neutralized with sodium carbonate and the solution concentrated in vacuo and dissolved in about 300 ml. of boiling 1N hydrochloric acid. This solution is diluted in about 300 ml. of water, cooled to about 5°C, filtered, and made basic with ammonia to precipitate the product. The product is collected and may be recrystallized from a dioxane hexane solution to yield the pure derivative of formula I.

The oxindole diamine derivatives of formula I of this invention may be used to prepare polyimides as described, for example, in our co-pending Patent Application No. 55195/72 (Serial No. 1419783).

To further illustrate this invention and the process employed in preparing the oxindole diamine derivatives, the following Examples are given below:

#### Example 1

3,3 - di - (p - aminophenyl) - 1 - phenyl-oxindole

(a) Preparation of 1-phenylisatin

To a solution of 1590 g (12.5 moles) of oxalyl chloride in 20 l. of dry methylene chloride at 0° was added, with stirring, a solution of 2115 g (12.5 moles) of diphenylamine in 10 l. of dry methylene chloride.

After the addition was completed, the mixture was brought to room temperature and

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5 stirred for 18 hours. The solution was then concentrated in vacuo. The residual oil was taken up in 30 l. of nitrobenzene, and this solution was treated with 3340 g (25 moles) of aluminium chloride. This solution was then heated, with stirring, at 120°C. for 4 hours. Vigorous hydrogen chloride evolution occurred throughout this operation.

10 (b) Preparation of 3,3 - di - (p - amino-phenyl)-1-phenyloxindole

The cooled solution from step (a) was treated with 3000 g (14.1 moles) of s-diphenylurea and an additional 3340 g (25 moles) of aluminium chloride. The mixture was maintained, with stirring, at 100°C for 18 hours.

20 The cooled solution was poured, with vigorous stirring, into a mixture of 100 l. of hexane and 100 l. of water. The precipitated solid was collected and washed with 10 additional litres of hexane to remove all residual nitrobenzene.

25 The collected solid was suspended in 50 l. of acetic acid and treated with 0.5 l. of water and 9.1 of concentrated sulphuric acid. The mixture, which became homogeneous on heating, was then refluxed for 18 hours.

30 The cooled solution was filtered, and the filter cake was washed with 2 l. of acetic acid. The combined filtrates were then treated carefully with 16 kg. of sodium carbonate and concentrated, in vacuo, to dryness. The remaining solids were taken up in 100 l. of boiling 1 N hydrochloric acid. The solution was cooled and filtered.

35 The filtrate was made basic with concentrated ammonium hydroxide and the precipitated solid was collected.

40 The crude diamine was recrystallized from 50 l. of methyl cellosolve with Darco decolorization (1 kg.) and water (70 l.) precipitation. The product had a melting point of 276—278°C. ["Cellosolve" and "Darco" are registered trade marks].

45 Calc. for  $C_{26}H_{21}N_3O$ :

Calculated:

%C, 79.77; %H, 5.41; %N, 10.74

Found:

%C, 78.87; %H, 5.65; %N, 10.45

50 By essentially following the above procedure in steps (a) and (b) and substituting for diphenyl amine in step (a), an equivalent amount of the following:

- 55 1. N-methylaniline  
2. N-propylaniline  
3. N-pentylaniline  
4. N-hexylaniline

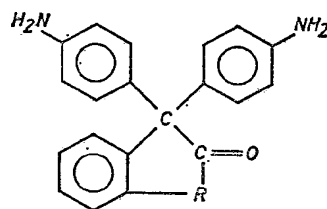
there was respectively obtained:

1. 3,3 - di - (p - aminophenyl) - 1 - methyl-oxindole 60  
2. 3,3 - di - (p - aminophenyl) - 1 - propyl-oxindole  
3. 3,3 - di - (p - aminophenyl) - 1 - pentyl-oxindole  
4. 3,3 - di - (p - aminophenyl) - 1 - hexyl-oxindole 65

In the procedure of Example 1, the respective oxindole diamine derivatives may be prepared by substituting for s-diphenylurea, an equimolar equivalent amount of the following anilides; acetanilide, propionanilide, pentananilide, hexananilide and benzanilide. 70

WHAT WE CLAIM IS:—

1. A compound having the formula:—



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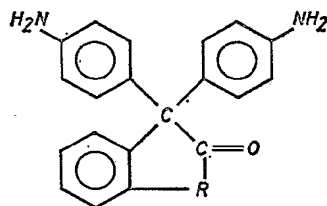
wherein R is an N-(lower)alkyl or an N-aryl residue.

2. A compound as claimed in Claim 1, wherein R is N-phenyl, or N-methyl.

3. 3,3 - Di - (p - aminophenyl) - 1 - phenyloxindole. 80

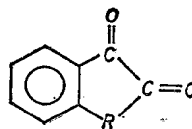
4. A compound of formula I as defined in Claim 1, substantially as described with reference to Example 1.

5. A process for preparing a compound having the formula: 85

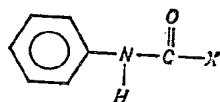


wherein R is an N-(lower)alkyl or an N-aryl residue, comprising the following steps:—

(a) reacting an isatin derivative of the formula 90



wherein R is S, N—H, an N-(lower)alkyl or an N-aryl residue with an anilide of the formula



- 5 wherein, X is an alkyl residue of from 1 to 6 carbon atoms or an aryl or anilino residue in the presence of a Friedel-Crafts catalyst in an inert solvent at a temperature of from 50°C. to 150°C., the isatin derivative being present in an amount ranging from 1% to 15% by weight of the total reaction mixture, the anilide being present in at least a mole equivalent amount based on the amount of the isatin derivative, and the Friedel-Crafts catalyst being present in an amount ranging from 2 to 10 mole equivalents based on the amount of the isatin derivative present in the reaction mixture;
- 10 (b) Precipitating the resultant reaction product from step (a) by dilution with a solvent which is not a solvent for the reaction product from step (a);
- 15 (c) hydrolyzing the reaction product in an aqueous acidic solution.
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6. A process as claimed in claim 5 wherein the solvent in step (b) is water, an aliphatic alkane or a mixture thereof.

7. A process as claimed in Claim 5 or 6 wherein R is N-phenyl or N-methyl.

8. A process as claimed in Claim 7 wherein R is N-phenyl and X is anilino.

9. A process as claimed in Claim 5 wherein the process is carried out in nitrobenzene at a temperature of from 90°C to 120°C; the concentration of the isatin derivative is between 2% and 7% by weight of the total reaction mixture; and the Friedel-Crafts catalyst is aluminium chloride.

10. A process according to Claim 5 wherein the aqueous acidic solution comprises acetic acid, water and sulphuric acid.

11. A process as claimed in Claim 5 substantially as described with reference to Example 1.

12. A compound of formula I as defined in Claim 1 when produced by a process claimed in any of Claims 5 to 11.

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